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Another "New" Form, the Palagonia Type of Acrofacial Dysostosis in a Sicilian Family

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We describe another previously apparently unreported form of acrofacial dysostosis (AFD) from Sicily, residing, coincidentally in the same small village as that with the recently delineated Catania AFD. In contradistinction to the latter, the 4 patients with the Palagonia form of AFD are of normal intelligence, and instead of extensive caries have oligodontia (4), short stature (3), frizzy hair (pili torti) with aplasia cutis verticis (1), mild cutaneous syndactyly of digits 2–5 (4), attenuation of the 4th metacarpals (3/3), unilaterally cleft lip (1), and some vertebral anomalies such as a large atlas (1), mild scoliosis (1), small odontoid process, spina bifida occulta at S1 (1). Causally, this would appear to be an iceberg dominant disorder, with the proposita most severely affected. This could be an X-linked dominant, but more likely an autosomal dominant trait. Am. J. Med. Genet. 69:388–394, 1997.

KEY WORDS: acrofacial dysostosis; aplasia cutis verticis; pili torti; syndactyly; oligodontia; dominant inheritance

INTRODUCTION

The recently delineated Catania form of acrofacial dysostosis [Opitz et al., 1993] was confirmed as nosologic entity by Wulfsberg et al. [1996]. Other forms of acrofacial dysostosis (AFD) were delineated by Medeira and Donnai [1994], Christianson et al. [1994] and Preis et al. [1995]; these appear to be lethal entities. However, recently, we were privileged to study a family with a previously apparently undescribed non-lethal form of acrofacial dysostosis originating, probably by coincidence, in the same village as the family with the original Catania form of acrofacial dysostosis.

CLINICAL REPORTS

The proposita (patient 1) is the second of 3 sibs, all affected, born to non-consanguineous parents. These were their only pregnancies. The mother appears to be mildly affected.

She was born with a birthweight of 4,200 g and two symmetrical areas of aplasia cutis (2 × 1 cm) on the vertex. Psychomotor development was normal, but growth was slow; at age 11 years she was evaluated for short stature.

On examination the proposita was in good health. Weight was 31 kg (50th centile), height 126 cm (3rd centile), OFC 57 cm (97th-centile). She had abundant, "frizzy"—curly hair with low posterior hairline, two (2 × 2 cm) symmetrical areas of headed aplasia cutis verticis, a wide, prominent forehead, thin eyebrows (sparse in the medial region), mild downslant of palpebral fissures, ectropion of lower lids with virtual absence of lower eyelashes, and malar hypoplasia with prominent tip of nose (Fig. 1a,b). Upper lip was short, philtrum relatively flat and she had microretrognathia. Lower height of face was disproportionately less than the upper. The auricles were apparently low-set and posteriorly angulated. She had a short neck and short hands with mild partial cutaneous syndactyly between fingers 2–5 (Fig. 2). Nails were normal. Dermatoglyphic finding include (R): 3W, 2U, triradius *t,* more medial position of triradius *b* and *d* than normal, second interdigital distal loop and hypothenar pattern; (L): 2W, 1R, 2U, a, b, c, d interdigital triradii, 4th interdigital distal loop, *t'* triradius and hypothenar distal radial loop. There was mild asymmetry of leg length.

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Fig. 1. **a,b:** Patient 1: Note bilateral ectropion of lower lids; sparse brows; malar hypoplasia; microretrognathia; curly, frizzly hair; reduced lower facial height.

Oral examination (Fig. 3a) showed a thick, short upper midline labio-gingival frenulum, a slight unilateral cross-bite, overjet and overbite. A supernumerary tooth was fused on the buccal surface of tooth 21 (left upper central incisor). Panorex film showed absence of the 4 premolars and of the right upper lateral incisor (Fig 3b,c). Palate is normal.

Intelligence was normal. Results of all routine lab tests were normal. Cephalometric films (Fig. 4a,b) showed a large atlas and slightly obtuse mandibular angle; in addition, she had delayed bone age (9 y), short and thin 4th metacarpals especially on the left (Fig. 4c); slight scoliosis and spina bifida occulta at S1. Trichoscopy showed pili torti.

Thus, this normally intelligent girl has: shortness of stature, a form of acrofacial dysostosis with oligodontia, mild interdigital webbing of fingers, aplasia cutis, pili torti and mild vertebral anomalies.

The older brother (patient 2) is 16 years old, 162 cm tall (<3rd centile), weighs 62 kg (50th centile), has an OFC of 58 cm (97th centile). A right cleft of upper lip

Fig. 2. Patient 1: Partial cutaneous syndactyly between 2nd, 3rd, 4th and 5th fingers.

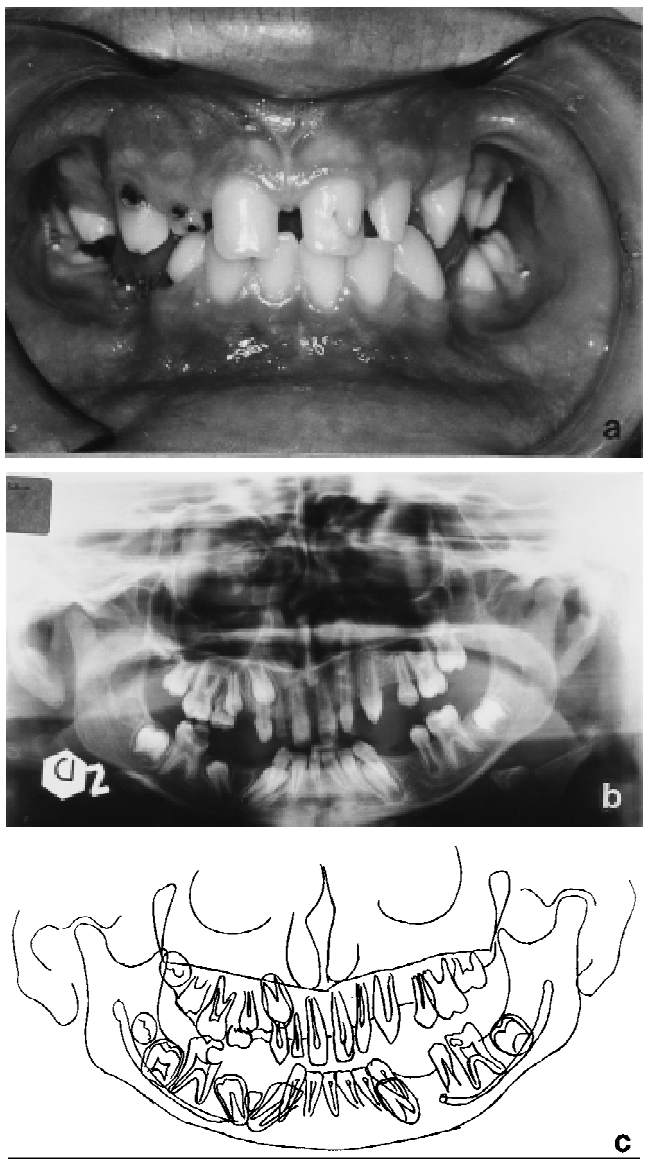

Fig. 3. **a,b,c:** Patient 1: Hypodontia and supernumerary tooth (a); absence of four premolars and lateral upper incisor (b,c).

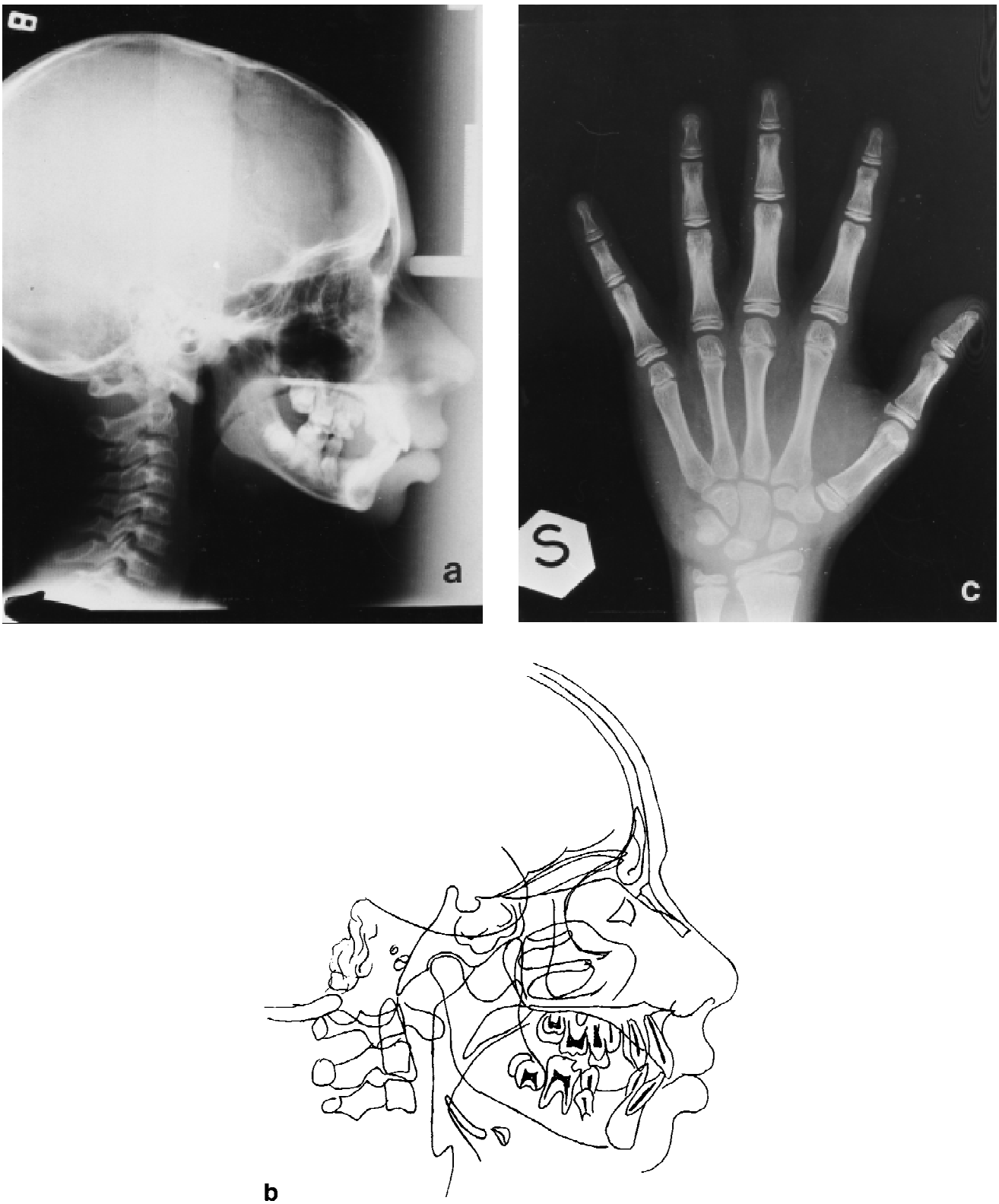

Fig. 4. **a,b,c:** Patient 1: Oligodontia, atlas hypertrophy (a,b); thin 4th metacarpal, delayed skeletal age (c).

Fig. 5. **a,b:** Patient 2: Note malar hypoplasia, scar of right upper lip.

was corrected at the age of 3 years. Like his sister, this young man had laterally sparse eyebrows (Fig. 5a,b), mild malar hypoplasia, small ears, absence of several teeth (first premolars and right upper lateral incisor) in addition to a lip scar, high arched palate and bilateral interdigital webbing between fingers 2–5. His hair is normal and he has no cutaneous or nail abnormalities. Intelligence is normal. Roentgenograms showed a small odontoid process, right mandibular ramus longer than left, left mastoid process larger than right, absence of teeth mentioned above, multiple dental diastemata especially in the upper arch, and a probable cyst in the left maxillary sinus (Fig. 6a,b). Hand films demonstrated mild shortness and thinness of the 4th metacarpals (Fig. 7). On dermatoglyphic analysis he mostly had ulnar loops (8) (with one whorl and one radial loop) on fingertips, *t* triradii, and a third interdigital loop on the right palm.

Thus, except for pili torti and aplasia cutis verticis this young man has a condition very similar to that of his older sister.

His younger sister (patient 3) is 3 9/12 years old and

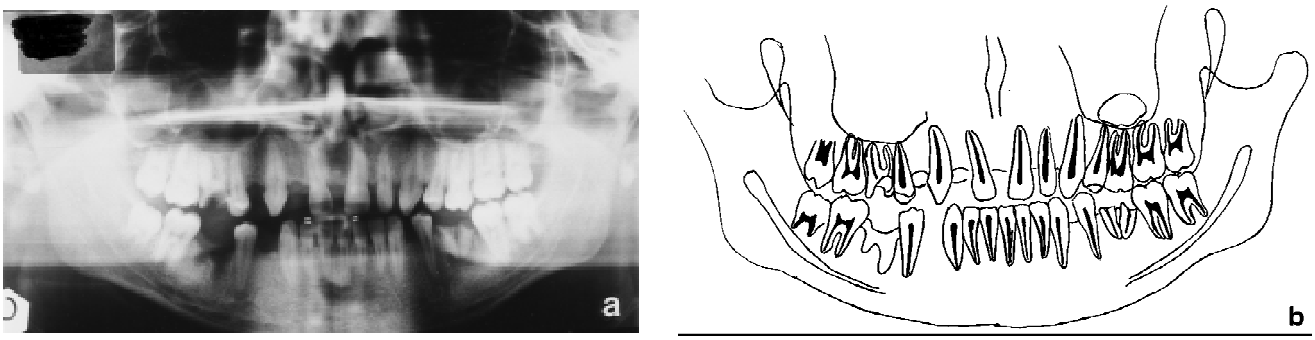

Fig. 6. **a,b:** Patient 2: Multiple diastemata; first premolars and right lateral incisor absent.

Fig. 7. Patient 2: Attenuation of fourth metacarpal.

Fig. 9. Patient 3: Attenuation of 4th metacarpal and of first phalanx of 5th digit.

Fig. 8. **a,b:** Patient 3: Malar hypoplasia; retrognathia, reduced mid face height.

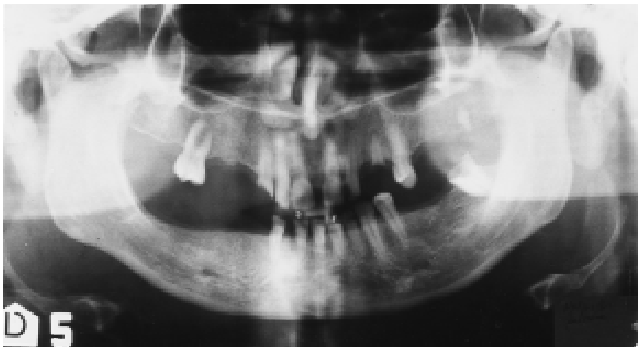

Fig. 10. Patient 4: Agenesis of upper lateral incisors.

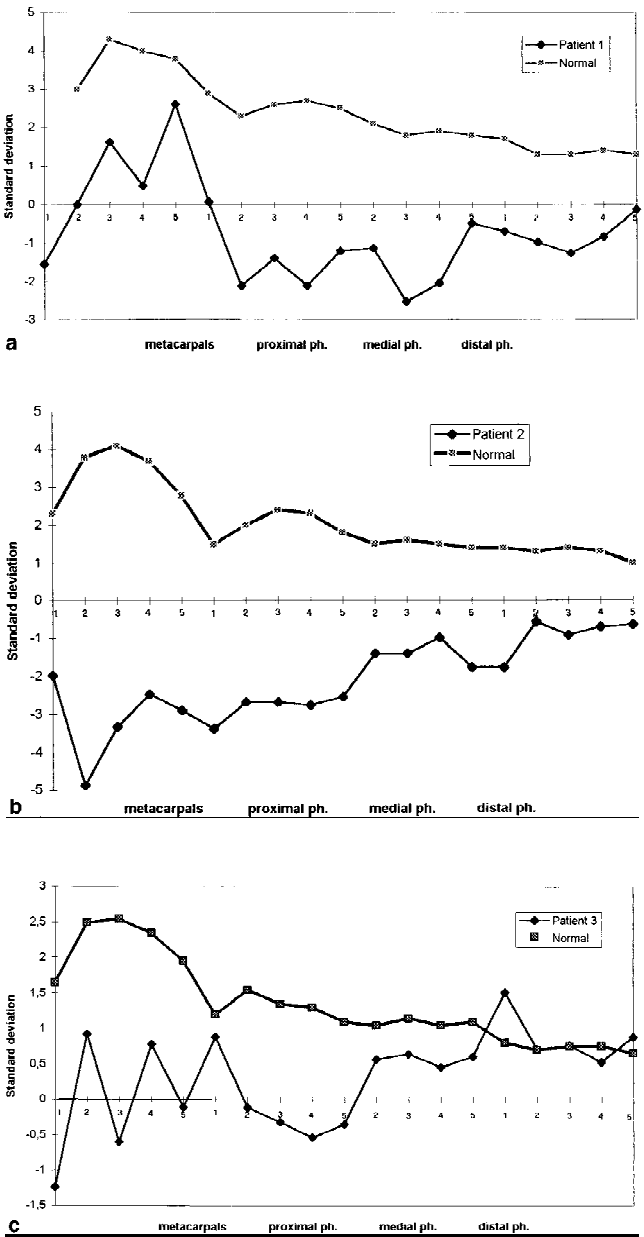

Fig. 11. **a,b,c:** Metacarpophalangeal profiles on patients 1, 2, 3.

of normal stature and weight (98 cm, 75th centile; 14.4 kg, 50th centile) with normal head size (49.2 cm, 50th centile) and normal intelligence. She has a striking resemblance to her older sibs (Fig. 8a,b) with equally prominent forehead, sparse eyebrows, reduced height of lower face, micrognathia, relatively pronounced nasolabi folds, flat philtrum, mild malar hypoplasia and mild interdigital webbing between all fingers. Dermatoglyphic findings include: no thenar patterns, *t* triradii, left hypothenar distal radial loop, normal *a b c d* triradii, left 4th and right 3rd interdigital distal loops. On fingertips ulnar loops (5), radial loops (2), whorls and one (tended) arch.

Hand films (Fig. 9) shows slight attenuation of the width of metacarpal 4 and of the first phalanges of the 5th digits.

The mother (patient 4) of these children is 39 years old and shows only mild malar hypoplasia, interdigital webbing, absence of upper lateral incisors (Fig. 10), overjet and overbite with normal palate and normal height for a Sicilian woman. The mother's parents were unavailable for examination, but are normal by history; family photos of the grandparents seem to confirm that supposition.

DISCUSSION

These four individuals are clearly abnormal, clearly have the same autosomal or X-linked dominant condition which is clearly different from the Catania form of acrofacial dysostosis notwithstanding origin in the same small Sicilian village (Palagonia, the families are unrelated). The condition is characterized by shortness of stature, normal IQ, mild acrofacial dysostosis (malar hypoplasia, mandibulo-micrognathia, webbing of digits with attenuation of the 4th metacarpals) with normal or high arched palate, oligodontia, and mild vertebral anomalies, aplasia cutis verticis and pili torti in one sib and cleft lip in another. Such an entity seems not to have been described before, although the manifestations in one patient share some similarity with those of a family described by Martinez et al. [1987] and another reported by Richieri-Costa et al. [1992], both considered to represent a new form of ectodermal dysplasia. In the first, signs of mandibulofacial dysostosis were inconspicious, and there was syndactyly of the first two digits. In the latter there was hypohidrosis without hypothermia and marked hypoplasia of toe nails without clear signs of mandibulofacial dysostosis. Our patients did not have nail abnormalities, hypohidrosis or preaxial syndactyly.

REFERENCES

Christianson AL, Kruger H, Dini L (1994): Atypical acrofacial dysostosis syndrome. Am J Med Genet 51:32–34.

Martinez BR, Monasterio LA, Pinheiro M, Freire-Maia N (1987): Cleft lip/palate-oligodontia-syndactyly-hair alterations, a new syndrome:

Review of the conditions combining ectodermal dysplasia and cleft lip/palate. Am J Med Genet 27:23–31.

Medeira A, Donnai D (1994): Postaxial acrofacial dysostosis syndrome with vertebral segmentation defects. Clinical Dysmorphol 3:171–174.

Preis S, Raymaekers-Buntinx I, Majewski F (1995): Acrofacial dysostosis of unknown type: Nosology of the acrofacial dysostoses. Am J Med Genet 56:155–160.

Opitz JM, Mollica F, Sorge G, Milana G, Cimino G, Caltabiano M (1993): Acrofacial dysostoses: Review and report of a previously undescribed condition: The autosomal or X-linked dominant Catania form of acrofacial dysostosis. Am J Med Genet 47:660–670.

Richieri-Costa A, Guion-Almeida ML, Freire-Maia N, Pinheiro N (1992): Autosomal recessive cleft/lip, ectodermal dysplasia, and minor acral anomalies: report of a Brazilian family. Am J Med Genet 44:158–162.

Wulfsberg BA, Supovitz KR, Campbell AB, Lurie IW (1996): Confirmation of the Catania brachydactylous type of acrofacial dysostosis: Report of a second family. Am J Med Genet 63:554–557.